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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	17

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/234,182	Hsei et al.
Examiner	**Group Art Unit**
Marianne DiBrino	1644

X Responsive to communication(s) filed on *Nov 22, 2000*

X This action is **FINAL.**

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

X Claim(s) *1-7, 19-22, 26-29, and 31-36* is/are pending in the applicat

Of the above, claim(s) *2-4, 6, 7, 20, 22, and 27* is/are withdrawn from consideration

Claim(s) _____ is/are allowed.

X Claim(s) *1, 5, 19, 21, 26, 28, 29, and 31-36* is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* X None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a))

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). 4, 5, 6

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's amendment filed 11/22/00 is acknowledged and has been entered.

2. Applicant's confirmation of election without traverse of a conjugate consisting of one Fab' antibody fragment attached to no more 10 non-proteinaceous polymer molecules which has a specific apparent size of at least about 500kD and at least about 8 fold greater than the apparent size of at least one antibody fragment, and a single chain PEG molecule of an average molecular weight of at least about 20kD is acknowledged.

Claims 2-4, 6, 7, 20, 22 and 27 stand withdrawn from further consideration by the Examiner, 37 C.F.R. 1.142(b), as drawn to non-elected species.

Claims 1, 5, 19, 21, 26, 28, 29, 31-35 and newly added claim 36 are presently being acted upon.

3. It is noted by the Examiner that Applicant has listed the references for the information disclosure statements filed 12/22/99, 10/26/99 and 6/08/99 in Applicant's transmittal letter of 11/22/00. However, the references can not be located. Hence, the said information disclosure statements fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the reference cited therein have not been provided by Applicant. The information disclosure statements have been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing elements will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

<u>The following are new grounds of rejection necessitated by Applicant's amendment filed 11/22/00.</u>

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 5, 19, 21, 26, 28, 29 and 31-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the broadly claimed conjugate.

The instant claims encompass a conjugate consisting of an antibody fragment that does not bind antigen covalently coupled to any polymer. There is insufficient disclosure in the specification for such a conjugate.

Applicant's arguments in the amendment filed 11/22/00 have been fully considered but are not persuasive.

It is Applicant's position on pages 6 and 7 under "Written Description" that the ability of the claimed conjugate to bind antigen is not needed for the conjugate to function as a toleragen for the underivatized parental antibody fragment and Applicant cites Wie for a description of how to use PEGylated allergen for the induction of tolerance to underivatized allergen in an animal.

It is the Applicant's position that Wie describes the tolerization of allergen rather than of an antibody and that claims 26, 28 and 29 require that the antibody fragment binds to the antigen. It is the Examiner's further position that the fab' antibody fragment recited in the instant claims, including those recited in claims 26, 28 and 29 may not in fact bind antigen and may not tolerize because the conformation of the molecule may be vastly different from that of the native molecule due to absence of the disulfide bond between the two chains.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1, 5, 19, 21, 26, 28, 29 and 31-36 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 5, 19, 21, 26, 28, 29 and 31-36 are indefinite in the recitation of "consisting essentially of" because it is not clear what other elements are encompassed that would not effect the basic and novel characteristics of the claimed invention. This term is considered indefinite when used in a compound claim.

Applicant's arguments in the amendment filed 11/22/00 have been fully considered but are not persuasive.

It is Applicant's position on pages 7-10 beginning at "Rejections under 35 USC second paragraph" that "consisting essentially of" is not indefinite because the phrase excludes ingredients that would materially affect the basic and novel characteristics of the claimed composition. Applicant cites 224 USPQ 409.

It is the Examiner's position that the claims of 224 USPQ 409 were drawn to a composition, whereas the claims of the instant application are drawn to a compound.
application.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

9. Claims 1, 5, 19, 21, 26, 28, 29 and 31-36 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,133,426.

U.S. Patent No. 6,133,426 discloses a conjugate comprising a fab' covalently attached to a PEG, wherein the PEG has an average molecular weight of at least about 20kD, wherein the said conjugate has an apparent size of at least about 500kD, i.e., at least about 8 fold greater than the apparent size of the antibody fragment, and wherein the PEG is attached to a cysteine residue in the light or heavy chain of the antibody fragment that would ordinarily form the disulfide bridge linking the light and heavy chains, wherein the disulfide bridge is avoided by substituting another amino acid , such as serine, for the corresponding cysteine residue in the opposite chain (especially column 15 at lines 23-51, column 16 at lines 25-47 and column 24 at lines 46-58). U.S. Patent No. 6,133,426 further discloses that the fab' can comprise a humanized anti-human IL-8 antigen binding site, including the complementarity determining regions of a light chain polypeptide amino acid sequence that is either 6G4V11N35A or 6G4V11N35E (especially column 15 at lines 52-67, column 16 at lines 1-6, column 74 at lines 18-26, and claims). U.S. Patent No. 6,133,426 also discloses conjugates further comprising

avidin or biotin, i.e., non-proteinaceous label molecules (especially column 84 at lines 9-19) or radiolabels (especially column 96 at lines 20-31). U.S. Patent No. 6,133,426 discloses use of the said conjugates for treatment of inflammatory disorders (especially Abstract). Instant claims 33 and 34 are included in this rejection because U.S. Patent No. 6,133,426 discloses that, unless specifically indicated to the contrary, "conjugate" is defined as a heterogeneous molecule formed by the covalent attachment of one or more antibody fragment(s) to one or more polymer molecule(s) (especially column 12 at lines 56-60), i.e., it is an inherent property of the conjugate that it's covalent structure is free of any matter other than the antibody fragment(s) and the polymer, i.e., PEG, molecule(s).

The reference teachings anticipate the claimed invention.

10. Claims 1, 5, 19, 21, 26, 28, 29 and 31-36 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,025,158.

U.S. Patent No.6,025,158 discloses a conjugate comprising a fab' covalently attached to a PEG, wherein the PEG has an average molecular weight of at least about 20kD, wherein the said conjugate has an apparent size of at least about 500kD, i.e., at least about 8 fold greater than the apparent size of the antibody fragment, and wherein the PEG is attached to a cysteine residue in the light or heavy chain of the antibody fragment that would ordinarily form the disulfide bridge linking the light and heavy chains, wherein the disulfide bridge is avoided by substituting another amino acid , such as serine, for the corresponding cysteine residue in the opposite chain (especially column 15 at lines 23-51, column 16 at lines 15-48 and column 24 at lines 30-55). U.S. Patent No.6,025,158 further discloses that the fab' can comprise a humanized anti-human IL-8 antigen binding site, including the complementarity determining regions of a light chain polypeptide amino acid sequence that is either 6G4V11N35A (especially column 15 at lines 52-67, column 16 at lines 1-6, column 80 at Table 1). U.S. Patent No. 6,133,426 also discloses conjugates further comprising avidin or biotin, i.e., non-proteinaceous label molecules (especially column 83 at lines 48-50) or radiolabels (especially column 95 at lines 55-67). U.S. Patent No. 6,025,158 discloses use of the said conjugates for treatment of inflammatory disorders (especially Abstract). Instant claims 33 and 34 are included in this rejection because U.S. Patent No. 6,025,158 discloses that, unless specifically indicated to the contrary, "conjugate" is defined as a heterogeneous molecule formed by the covalent attachment of one or more antibody fragment(s) to one or more polymer molecule(s) (especially column 12 at lines 53-58), i.e., it is an inherent property of the conjugate that it's covalent structure is free of any matter other than the antibody fragment(s) and the polymer, i.e., PEG, molecule(s).

The reference teachings anticipate the claimed invention.

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1, 5, 19, 21, 26, 28, 29 and 31-36 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,133,426. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 5, 19, 21, 26, 28, 29 and 31-36 recite limitations, (i.e., a conjugate comprising a fab' covalently attached to a PEG, wherein the PEG has an average molecular weight of at least about 20kD, wherein the said conjugate has an apparent size of at least about 500kD, i.e., at least about 8 fold greater than the apparent size of the antibody fragment, and wherein the PEG is attached to a cysteine residue in the light or heavy chain of the antibody fragment that would ordinarily form the disulfide bridge linking the light and heavy chains, wherein the disulfide bridge is avoided by substituting another amino acid , such as serine, for the corresponding cysteine residue in the opposite chain (especially column 15 at lines 23-51, column 16 at lines 25-47 and column 24 at lines 46-58). U.S. Patent No. 6,133,426 further discloses that the fab' can comprise a humanized anti-human IL-8 antigen binding site; conjugates further comprising avidin or biotin, i.e., non-proteinaceous label molecules (especially column 84 at lines 9-19) or radiolabels (especially column 96 at lines 20-31) or leucine zippers (especially column 84 at lines 48-54); SEQ ID NO: 60 and 70) that are disclosed in U.S. Patent No. 6,133,426.

13. Claims 1, 5, 19, 21, 26, 28, 29 and 31-36 are directed to an invention not patentably distinct from claim of commonly assigned U.S. Patent No. 6,133,426. Specifically, claims 1, 5, 19, 21, 26, 28, 29 and 31-36 are not patentably distinct for the reasons enunciated supra in item #12 of this Action.

14. Commonly assigned U.S. Patent No. 6,133,426, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.
A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g).

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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April 20, 2001

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